

In re application of: SIFFERT,  
Application No.: Not yet assigned  
Filed: Herewith

Group:  
Examiner:

Not assigned  
Not yet assigned

(Continuation of 09/180,783 - Filed: 17 March 1999)

2329-2333). The coding region has an Ser codon (TCC) at position 275, while subjects with an increased risk of a disease associated with G protein dysregulation have the codon TCT, which likewise codes for Ser, at this position. The genetic modification is a base substitution at position 825 in which a cytosine (C) is replaced by thymine (T). However, this base exchange is "silent" at the amino-acid level, ie. It does not lead to incorporation of a different amino acid at this position. The sequence found in subjects with an increased risk of disease is depicted in SEQ ID NO:1 in the sequence listing.

**IN THE CLAIMS:**

Please cancel claims 2 -12 and add new claims 13-31 as follows:

13. A method of diagnosing a disease comprising determining the presence of a genetic modification in a gene obtained from a subject which encodes a human G protein  $\beta_3$  subunit.
14. The method as claimed in Claim 13, wherein said disease is a disorder associated with G protein dysregulation.
15. The method as claimed in Claim 13, wherein said gene which encodes a human G protein  $\beta_3$  subunit is the gene of SEQ ID NO: 1.
16. The method as claimed in Claim 15, wherein the genetic modification is in the codon for amino acid 275 in SEQ ID NO: 1.
17. The method as claimed in Claim 16, wherein the genetic modification is a substitution of cytosine by thymine at position 825 in SEQ ID NO: 1.

18. The method as claimed in Claim 14, wherein the disorder is a cardiovascular disease, a metabolic disturbance or an immunological disease.
19. The method as claimed in Claim 14, wherein the disorder is hypertension.
20. A method for establishing the relative risk of developing a disorder associated with G protein dysregulation for a subject, comprising the steps of:
- (I) determining the presence of a genetic modification in a gene obtained from a subject which encodes a human G protein  $\beta_3$  subunit;
  - (II) in the event the presence of a genetic modification is determined, assigning the subject an increased risk of disease.
21. The method as claimed in Claim 20, comprising comparing said gene obtained from a subject which encodes a human G protein  $\beta_3$  subunit to the gene sequence of SEQ ID NO: 1.
22. The method as claimed in Claim 21, wherein the genetic modification which is determined is the presence of a thymine (T) at position 825 in the gene obtained from the subject.
23. The method as claimed in Claim 20, wherein the presence of a genetic modification in the gene obtained from a subject is determined by sequencing.
24. The method as claimed in Claim 23, further comprising the step of amplifying the gene obtained from the subject before sequencing.
25. The method as claimed in Claim 23, wherein a section the gene from the host corresponding to position 825 in the gene of SEQ ID NO: 1 is amplified.

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26. The method as claimed in Claim 20, wherein the presence of a genetic modification in the gene obtained from the subject is determined by hybridization.
27. The method as claimed in Claim 20, wherein the presence of a genetic modification in the gene obtained from the subject is determined by cleavage using a restriction enzyme.
28. The method as claimed in Claim 27, wherein the restriction enzyme is Dsa I.
29. A non-human transgenic animal comprising a gene which encodes a modified human G protein  $\beta_3$  subunit.
30. The non-human transgenic animal as claimed in Claim 29, which encodes a modified human G protein  $\beta_3$  subunit of SEQ ID NO: 1.
31. The non-human transgenic animal as claimed in Claim 30, wherein said modified human G protein  $\beta_3$  subunit includes a substitution of cytosine with thymine at position 825.

**IN THE SEQUENCE LISTING:**

Please delete the Sequence Listing on pages 7-9 of the application, and insert the enclosed substitute Sequence Listing into the application.